Annual Surveillance Summary: *Acinetobacter* Infections in the Military Health System, 2015

NMCPHC-EDC-TR-291-2017

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Prepared May 2017

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ORGANIZATION.

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
May 2017	Technical Report	01 January 2015 - 31 December 2015

4. TITLE AND SUBTITLE
Annual Surveillance Summary: Acinetobacter Infections in the Military Health System (MHS), 2015

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Chelsea Stone, Uzo Chukwuma

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
EpiData Center
Navy and Marine Corps Public Health Center
620 John Paul Jones Circle, Suite 1100
Portsmouth, VA 23708-2103

8. PERFORMING ORGANIZATION REPORT NUMBER
NMCPHC-EDC-TR-291-2017

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
EpiData Center
Navy and Marine Corps Public Health Center
620 John Paul Jones Circle, Suite 1100
Portsmouth, VA 23708-2103

10. SPONSOR/MONITOR'S ACRONYM(S)
EDC, NMCPHC

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
NMCPHC-EDC-TR-291-2017

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The EpiData Center conducts routine surveillance of clinically significant organisms within the Department of the Navy and the Department of Defense (DOD) beneficiary populations. For calendar year (CY) 2015, this report summarizes incidence, prevalence, demographic and clinical characteristics, prescription practices, and antibiotic resistance patterns observed for Acinetobacter species infections identified within the Military Health System (MHS). Several data sources were linked to assess a variety of descriptive and clinical factors related to Acinetobacter species. In 2015, the Acinetobacter species incidence rate was 5.63 per 100,000 persons per year, which reflects a 10.91% increase from the weighted historic incidence rate. The majority of infections in 2015 were identified in the outpatient setting and manifested as skin and soft tissue and wound infections. Acinetobacter baumannii-calcoaceticus complex was the most common species isolated (29.3%). Overall incidence of multidrug-resistant Acinetobacter remains low in the DOD (0.3 per 100,000 persons per year). Overall, antibiotic susceptibilities remain high and relatively stable.

15. SUBJECT TERMS
Health Level 7 (HL7), microbiology, surveillance, Acinetobacter, Military Health System (MHS), multi-drug resistance (MDR), healthcare-associated infection (HAI), community-associated (CA) infection

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Uzo Chukwuma MPH
U	U	U	UU	28	19b. TELEPHONE NUMBER *(Include area code)* 757-953-0970

Reset

Standard Form 298 (Rev. 8/98)
Prescribed by ANSI Std. Z39.18
Adobe Professional 7.0

Abstract

The EpiData Center conducts routine surveillance of clinically significant organisms within the Department of the Navy and the Department of Defense (DOD) beneficiary populations. For calendar year (CY) 2015, this report summarizes incidence, prevalence, demographic and clinical characteristics, prescription practices, and antibiotic resistance patterns observed for *Acinetobacter* species infections identified within the Military Health System (MHS).

Several data sources were linked to assess a variety of descriptive and clinical factors related to *Acinetobacter* species. Health Level 7 (HL7) formatted microbiology data were used to identify infections. Infections were matched to HL7-formatted pharmacy data to assess prescription practices, the Standard Inpatient Data Record to determine healthcare-associated exposures, Defense Manpower Data Center (DMDC) rosters to determine burden among DOD active duty service members, and the DMDC Contingency Tracking System to determine deployment-related infections.

In 2015, the *Acinetobacter* species incidence rate was 5.63 per 100,000 persons per year, which reflects a 10.91% increase from the weighted historic incidence rate. The majority of infections in 2015 were identified in the outpatient setting and manifested as skin and soft tissue and wound infections. *Acinetobacter baumannii-calcoaceticus* complex was the most common species isolated (29.3%). Overall incidence of multidrug-resistant *Acinetobacter* remains low in the DOD (0.3 per 100,000 persons per year). Overall, antibiotic susceptibilities remain high and relatively stable.

Contents

Background

Acinetobacter species are gram-negative bacteria that have shown significant increases in resistance to traditional antibiotics over the past several decades. The most clinically important *Acinetobacter* species are *A. baumannii*, *A. pttili (*genomic species 3), and *A. nosocomialis* (genomic species 13TU), which are associated with a large number of infections and demonstrate a remarkable ability to acquire resistance.[1-3] Using normal phenotypic tests, these three species, plus *A. calcoaceticus* (a common environmental organism not associated with clinically relevant disease), are difficult to distinguish from one another. Because genetic testing is not always practical, experts commonly refer to these four species as the *A. baumannii-calcoaceticus* complex, or ABC.[1-5]

Acinetobacter bacteria are biologically adept at surviving in a wide range of environments and conditions. *Acinetobacter* species are hydrophilic, widely distributed in water and soil, and grow at various temperatures and acidities.[5,6] These characteristics allow for significant risk of acquisition and transmission of novel infections and/or novel resistance strains.[5] The presence of prevalent multidrug-resistant (MDR) *Acinetobacter* species and ease of human travel around the globe also allow for the transmission of novel resistant strains into new environments.[7] In addition, certain climatic conditions facilitate the transmission of *Acinetobacter* species in the community setting as well as in the hospital environment, and *A. baumannii* strains known to infect humans have been isolated from animals, potentially suggesting that animals could establish a community reservoir.[6] Evidence of community carriage/reservoirs has only been discussed in the literature for the past 15 years and focuses only on single events or cases.[6]

Acinetobacter species are able to respond to antimicrobial pressure, and various strains have developed resistance to all currently available antibiotics.[7-9] One of the major mechanisms by which *Acinetobacter* develops resistance and persists in varied environments is its ability to produce biofilms that are difficult to control.[9] Although not completely understood, *Acinetobacter* species biofilms can adhere to abiotic, biotic, and clinically relevant surfaces such as hospital respirators, bed linen, telephones, door handles, polystyrene, and human epithelial cells.[5,9] According to Singh et al, *Acinetobacter* species biofilms have been linked with hospital-acquired infections, chronic non-healing injury, burn wound infections, ulcers, and battle casualties among military personnel.[9] *Acinetobacter*'s capability to survive for extended periods of time in the environment likely leads to transmission within the healthcare setting.[5,10] Cross-transmission of *Acinetobacter* species from patient to patient and the possibility of outbreak by patient transfer has been demonstrated.[6] Multiple European, North American, and Asian hospitals have reported outbreaks of *Acinetobacter* species isolates displaying multidrug resistance.[7] In particular, *A. baumannii* is frequently responsible for nosocomial pneumonia in intensive care units (ICUs), predominately ventilator-associated pneumonia.[10]

At particular risk for *A. baumannii* infection are military service members deployed to combat theaters of operation, especially those in the Middle East.[11-13] *A. baumannii* is rarely a component of normal human skin flora.[5] However, *Acinetobacter* species are occasionally found on the skin and in the throat and secretions of healthy people.[10] During the Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF), MDR *Acinetobacter* species infections occurred with greater

frequency in United States (US) service members injured in Middle Eastern countries compared to their counterparts stationed in the US.[6,13,14] During this period, *Acinetobacter* species infections were a major pathogen complicating combat injuries.[7]

It is important to monitor the epidemiology of *Acinetobacter* species on an ongoing basis. The following report summarizes the burden of *Acinetobacter* species infections for calendar year (CY) 2015 among Military Health System (MHS) beneficiaries. This report describes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns associated with *Acinetobacter* species infections among DOD MHS beneficiaries, as well as Department of the Navy (DON) active duty service members with deployment-related infections.

Methods

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducted retrospective surveillance of *Acinetobacter* species infection in the MHS in CY 2015 (01 January 2015 to 31 December 2015). Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data were used to identify positive *Acinetobacter* species laboratory results. A unique *Acinetobacter* species infection was defined as the first positive *Acinetobacter* species laboratory result per person per 30 days. Incidence represented the first unique infection per person per calendar year and prevalence was defined as all unique *Acinetobacter* species infections.

Demographic Classification

Demographic information for each incident infection was described using data within the HL7-formatted CHCS microbiology record. Infections were classified according to the patient's gender, age, sponsor service (Air Force, Army, Marine Corps, or Navy), beneficiary status (Active Duty, Retired, Family Member, or Other), and region of the facility where the specimen was collected. The Active Duty category included both active duty and recruit personnel, defined by the beneficiary type codes of 11 and 13, respectively.

Acinetobacter species incidence rates and prevalence infections were aggregated into six spatial regions and visualized as maps created in ESRI ArcGIS software (version 10.2.2). Organisms identified in each region may act as a reservoir within that region and contribute to the burden of exposure. Geographic regions were assessed within the continental United States (CONUS) and outside the CONUS (OCONUS), with the spatial regions identified as follows:

- **Northeast**: Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, Pennsylvania, New Jersey.
- **Midwest**: Michigan, Wisconsin, Minnesota, Ohio, Indiana, Illinois, Iowa, Missouri, Kansas, Nebraska, North Dakota, South Dakota.
- **West**: California, Oregon, Washington, Idaho, Montana, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Alaska, Hawaii.
- **South**: Texas, Oklahoma, Arkansas, Louisiana, Mississippi, Alabama, Tennessee, Kentucky.
- **South Atlantic**: Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida.
- **OCONUS**: All US territories and non-US countries.[15]

Clinical Characteristics Classification

Clinical characteristics were described for prevalent infections using information within the HL7-formatted CHCS microbiology record. Specimens were classified as inpatient or outpatient based on the Medical Expense and Performance Reporting System (MEPRS) codes of the location where the specimen was collected. A MEPRS code of A indicated specimen collection in the inpatient setting. All other MEPRS codes were considered outpatient encounters.

Infections were classified into invasive and non-invasive categories using the specimen source or body site variables in the HL7-formatted CHCS microbiology record. The terms used to group the data into these categories are described in Table 1. In addition, infections were further categorized based on body collection sites specific to the organism of interest (e.g., urine, respiratory, bloodstream) to provide enhanced granularity to the source of infection. Clinical characteristics were presented as a proportion of all infections within the population meeting the definition criteria.

Table 1. Invasive and Non-Invasive Infection Classification for *Acinetobacter* Species Infections Accessing the MHS

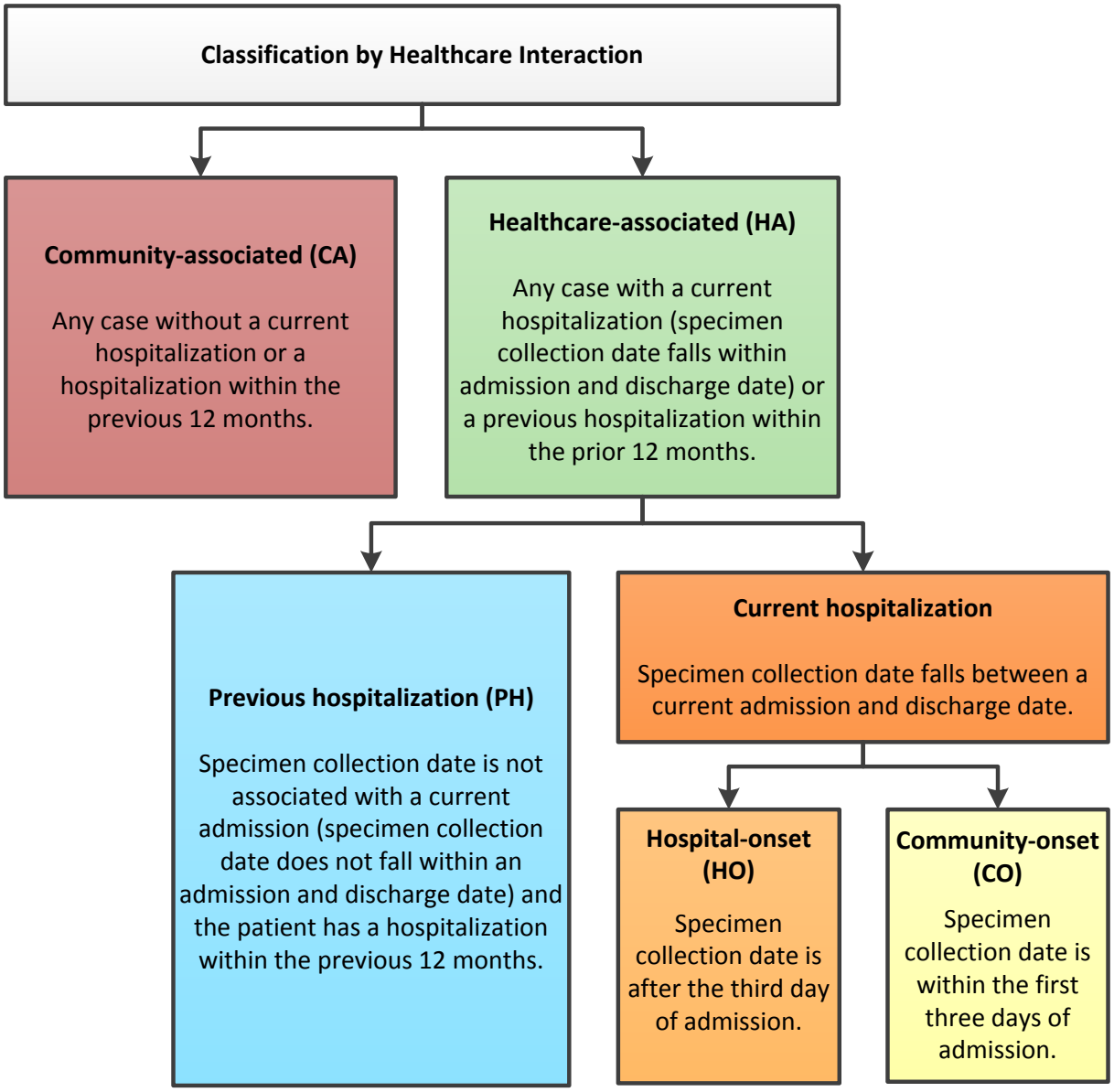
Infection Classification	If Body Site or Specimen Source Sample Taken From:
Invasive Infections	Blood, bone, cerebrospinal fluid, peritoneal fluid, pleural fluid, or synovial fluid
Other Non-Invasive Infections	Abscess, aspirate, body fluid, boil, bursa, carbuncle, cellulitis, cyst, discharge, drainage, exudate, eye, genital, lesion, pus, pustule, respiratory, skin, sputum, stool, swab, throat, tissue, urine, or wound

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Epidemiologic Infection Classification

To evaluate all laboratory-confirmed *Acinetobacter* species infections for recent contact with the healthcare system, *Acinetobacter* species prevalence infections were matched to the Standard Inpatient Data Record (SIDR) to determine epidemiologic infection classification. Records were categorized as either community-associated (CA) or healthcare-associated (HA). CA cases were defined as patients without a current hospitalization or a hospitalization in the previous 12 months. HA cases were defined as patients who were hospitalized at the time of infection (currently hospitalized) or who had a hospitalization within the previous 12 months. Current hospitalizations were further categorized as a hospital-onset (HO) case or a community-onset (CO) case. HO cases were defined as patients with an *Acinetobacter* species organism identified after the third day of the current admission. CO cases were identified as patients with a specimen collected within the first three days of the current admission yielding an *Acinetobacter* species organism, indicating the patient likely acquired the organism within the community and arrived at the treating facility with it.[16] Figure 1 presents the definitions for epidemiologic infection classifications.

Figure 1. Epidemiologic Infection Classifications[a]



[a]Cohen A, Calfee D, Fridkin SK, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infect Cont Hosp Ep*. 2008; 29(10):901-913. Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Exposure Burden Metrics

Only the first unique multidrug-resistant organism (MDRO) infection per patient per admission was used to analyze exposure burden metrics in the MHS. Admission prevalence estimated the exposure of infection at the time of admission (importation of MDROs into the MHS), which included MDROs isolated from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year. Overall prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, or samples that tested positive for infection in the prior calendar year. Admitted patients with a history of colonization or infection were identified by searching prevalence infection MDROs from the prior calendar year to determine a history of infection. These beneficiaries were counted in both the admission and overall prevalence populations as they contributed to the colonization pressure and exposure burden for those not already colonized or infected in both populations.[16] The historical review of data is included to show a reservoir of antimicrobial resistance and pressure among *Acinetobacter* species infections. Regional rates of exposure burden were calculated as the rate of exposure (admission or overall prevalence) per 1,000 inpatient admissions per region per year.

Pharmacy Transactions

To analyze antimicrobial prescription practices in the MHS, the HL7-formatted microbiology *Acinetobacter* species prevalence infections were matched to pharmacy data to identify antibiotic prescriptions associated with *Acinetobacter* species infections in all pharmacy databases (outpatient oral (OP), inpatient oral (unit dose, or UD), and inpatient and outpatient intravenous (IV)). Prescriptions were considered to be associated with an *Acinetobacter* species infection if the transaction date in the pharmacy record occurred either seven days before or after the date the results were certified in the laboratory data. All pharmacy transactions, regardless of database source (UD, IV, OP), were evaluated as one data source. Cancelled prescriptions or those with zero or null filled prescriptions were removed prior to analysis. A unique antibiotic prescription was defined as the first dispensed prescription for an antibiotic per prevalent infection. Antimicrobials recommended for treatment of *Acinetobacter* species infections according to the Johns Hopkins Antibiotic Guide were retained for analysis.[17]

Antimicrobial Resistance Classification

To evaluate changes in antimicrobial susceptibility for *Acinetobacter* species infections, an antibiogram was created using antibiotic susceptibility results from the microbiology record according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.[18] The antibiogram includes the first isolate per person per organism per year from 2010 to 2015. The Cochran-Armitage trend test was used to assess patterns in susceptibility across years. Trend direction for a single antibiotic over time was established using the two-tailed *P*-value; an increase in susceptibility was denoted by a green upward arrow and a decrease in susceptibility was denoted by a blue downward arrow. A statistically significant trend was established using a *P*-value ≤ 0.05.

Susceptibility results from the microbiology record were used to establish the level of antibiotic resistance among prevalent infections. Specimens that were non-susceptible (resistant or

intermediately susceptible) to at least one antibiotic from at least three different antibiotic classes were considered MDR. The antibiotic classes of interest in this classification included select aminoglycosides, antipseudomonal carbapenems, antipseudomonal fluoroquinolones, anti-pseudomonal penicillin β-lactamase inhibitors, extended spectrum cephalosporins, folate pathway inhibitors, penicillin + β-lactamase inhibitors, polymyxins, and tetracyclines. Possible extensively drug-resistant (PXDR) infections were those organisms non-susceptible to some antimicrobials tested in an antimicrobial category but not tested against all antimicrobial categories in the definition and could therefore not be included or excluded as an extensively drug-resistant (XDR) infection. Organisms that were non-susceptible to at least one antibiotic in all but one or two classes of nine total classes in the definition were considered XDR. Possible pandrug-resistant (PPDR) infections were those that could not be definitively identified as XDR based on the XDR definition and were non-susceptible to all antibiotics tested but were not tested against all antibiotics in the definition and could therefore not be excluded as a pandrug-resistant (PDR) infection. Finally, PDR organisms were organisms that were non-susceptible to all antibiotics in all antibiotic classes in the definition.[8] For the remainder of this report, unless otherwise stated, resistant and resistance are defined as *Acinetobacter* species infections having any level of antibiotic resistance, whether it be MDR, PXDR, XDR, PPDR, or PDR. See Appendix A (Table A1) for a list of antibiotics used to identify the level of resistance among infections.

Special Populations

Acinetobacter species infections identified among DON active duty personnel were matched to the Defense Manpower Data Center (DMDC) Contingency Tracking System (CTS) to explore deployment-related infections occurring on or between the start and end dates of the deployment plus 30 days. Thirty days post-end of deployment was used to ensure all *Acinetobacter* species infections related to the deployment were included. Records with no deployment end date (i.e., service member remains deployed) were also included provided that the infection occurred in the analysis year (2015) and the start date of deployment was within 180 days of the results certification date.

Statistical Analysis

The MHS Data Mart (M2) was used to obtain counts of TRICARE eligible MHS beneficiaries for denominators. The annual incidence rate was defined as the count of all incident infections per year divided by the corresponding annual M2 eligible beneficiary count (represented by the count in July) per year. A weighted average of incidence rates by month for the three years prior to the current analysis year (weighted historic monthly baseline) was used to assess the seasonal component of *Acinetobacter* species infections in 2015. One and two standard deviations, both above and below the weighted historic monthly baseline, were used to indicate statistically significant changes in incidence rates of *Acinetobacter* species infections in the analysis year.

All incidence rates are presented as an estimated rate per 100,000 persons per year. Due to the transient nature of the military beneficiary population and an inability to account for the proportion of the beneficiary population that receives medical care outside of the MHS, estimated rates are used for comparison of rates from year to year. A historical baseline was

created using the weighted average of the immediately preceding three years. The historical baseline of the incidence rate serves as a clinical reference for the 2015 incidence rate. Two standard deviations on either side of the baseline were calculated to assess variation in incidence rate in the three years prior to the current evaluation period. Two standard deviations provide the upper and lower bounds (approximately 95%) for assessing whether the observed occurrence was likely due to chance, and for consideration of clinically significant trends.

Results

Section A – Descriptive Epidemiology

Incidence of *Acinetobacter species*

In 2015, the annual incidence rate (IR) for *Acinetobacter* species infection was 5.63 per 100,000 persons per year for all MHS beneficiaries treated at a fixed military treatment facility (MTF). This reflects a 10.91% difference above the weighted historic baseline IR. The 2015 IR is above two standard deviations of the weighted historic baseline IR and therefore above expected rates for *Acinetobacter* species infections in the MHS population. The Air Force IR was also above two standard deviations of the weighted historic baseline IR. The IRs for the Army, Marine Corps, Navy, and DOD active duty populations were within two standard deviations of the weighted historic baseline (Table 2).

Table 2. Incidence Rate (IR) for *Acinetobacter* Species Infections in the MHS, CY 2015

Population	2015 IR	Weighted Historic[a] IR 2012 - 2014	Two Standard Deviations: Weighted Historic[a] IR	2015	
				Direction	Percent Change[b]
MHS Beneficiaries	5.63	5.08	0.28	↑	10.91%
Air Force	3.85	3.02	0.66	↑	27.44%
Army	5.55	5.13	0.58	↑	8.32%
Marine Corps	9.15	8.55	2.20	↑	7.01%
Navy	4.66	4.15	0.54	↑	12.11%
DOD Active Duty	11.34	9.25	3.50	↑	22.55%

Rates are presented as the rate per 100,000 persons per year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
[a] Historic IR reflects the weighted average of the three years prior to the analysis year.
[b] This reflects the percent change from the weighted historic IR to the IR of the current analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Demographic Distribution of *Acinetobacter species*

In 2015, there were 531 incident *Acinetobacter* species infections identified among all MHS beneficiaries treated at an MTF. By category, incidence rates were highest among males, active duty members, and individuals between the ages of 18-24 (Table 3).

Table 3. Demographic Characteristics of *Acinetobacter* Species Infections in the MHS, CY 2015

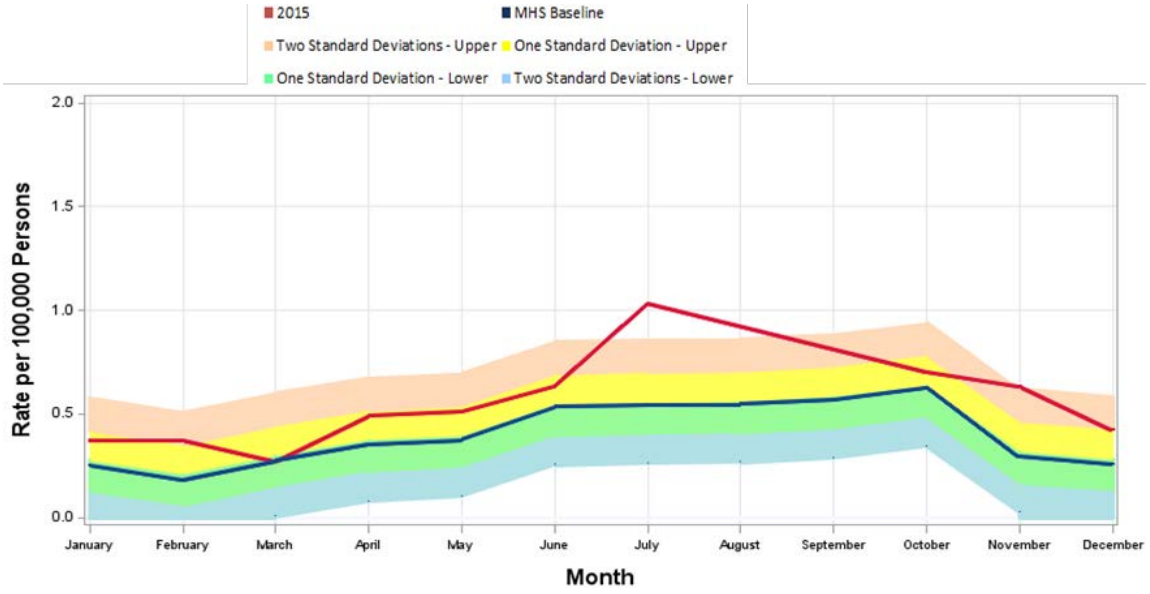
	N = 531	
	Count	**Rate**
Gender		
Female	208	4.5
Male	323	6.7
Age Group (in Years)		
0-17	78	4.0
18-24	127	11.0
25-34	77	6.4
35-44	52	6.2
45-64	101	4.8
65+	96	4.4
Beneficiary Type		
Active Duty	156	11.3
Family Members	209	3.8
Retired	82	3.8
Other[a]	84	--

[a] Rate is not reported due to variation in population denominator.
Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Seasonality

Throughout 2015, monthly incidence rates of *Acinetobacter* species infections were variable and usually fell within two standard deviations above the weighted historic baseline. With the exception of March, all monthly data points were above the weighted historic baseline. The highest rates occurred in July, August, and November and were more than two standard deviations above the weighted historic baseline incidence rate; these rates were therefore higher than expected for *Acinetobacter* species infections in the MHS population (Figure 2). Seasonal components of *Acinetobacter* species infections were observed in 2015, with the largest peak in incidence occurring in the summer. Incidence decreased into the fall and winter months.

Figure 2. Monthly Incidence of *Acinetobacter* Species Infections and Baseline Comparisons in the MHS, CY 2015



Rates are presented as the rate per 100,000 persons per year.
Bands indicate one and two standard deviations above and below the weighted historic monthly baseline.
The monthly baseline is a weighted average of the three years prior to the analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Acinetobacter Species Clinical Characteristics

There were 539 prevalent *Acinetobacter* species infections identified among all MHS beneficiaries treated at an MTF in 2015. The largest percentage of infections occurred in the outpatient setting (86.1%). The majority of *Acinetobacter* species infections were classified as non-invasive (86.5%). *Acinetobacter* species were identified from the following body collection sites: skin and soft tissue infection (SSTI)/wound (46.6%), urine (24.1%), respiratory (13.9%), and blood (6.1%). Samples collected outside of the listed body collection sites were reported collectively as an 'other' category. *A. baumannii calcoaceticus* complex (ABC) accounted for 29.3% of all infections followed closely by *Acinetobacter* species, not otherwise specified (NOS) (28.4%); *A. baumannii* (24.5%); and *A. lwoffi* (12.6%) (Table 4).

Table 4. Clinical Characteristics of *Acinetobacter* Species Prevalence Infections in the MHS, CY 2015

	N = 539	
	Count	Percentage
Specimen Collection Location		
Inpatient	75	13.9
Outpatient	464	86.1
Infection Type		
Invasive	73	13.5
Other Non-Invasive	466	86.5
Body Collection Site		
Blood	33	6.1
Respiratory	75	13.9
SSTI/Wound	251	46.6
Urine	130	24.1
Other	50	9.3
Organism Species		
Acinetobacter baumannii calcoaceticus complex	158	29.3
Acinetobacter species, NOS	153	28.4
Acinetobacter baumannii	132	24.5
Acinetobacter lwoffii	68	12.6
Acinetobacter haemolyticus	8	1.5
Acinetobacter junii	8	1.5
Acinetobacter radioresistens	7	1.3
Acinetobacter ursingii	5	0.9

Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Exposure Burden Metrics

Table 5 presents two different metrics defining *Acinetobacter* species counts for healthcare-associated exposures. The admission prevalence metric measures the magnitude of infection at the time of admission (importation of *Acinetobacter* species into the healthcare system) or one year prior, while the overall prevalence metric measures the exposure of infection at any point during the admission or one year prior. In 2015, the overall MDRO prevalence count for *Acinetobacter* species was 32, while the admission MDRO prevalence count for *Acinetobacter* species was 25. For both overall and admission MDRO prevalence, the US West region had the highest counts, accounting for nearly a third of all prevalence MDROs per metric.

Table 5. MDRO Healthcare-Associated Exposure Burden Metrics among *Acinetobacter* Species in the MHS, CY 2015

	Overall MDRO Prevalence[a]	Admission MDRO Prevalence[b]
	Count[c]	Count[c]
Region		
OCONUS	8	7
US Midwest	3	3
US Northeast	0	0
US South	7	5
US South Atlantic	5	2
US West	9	8
Total	32	25

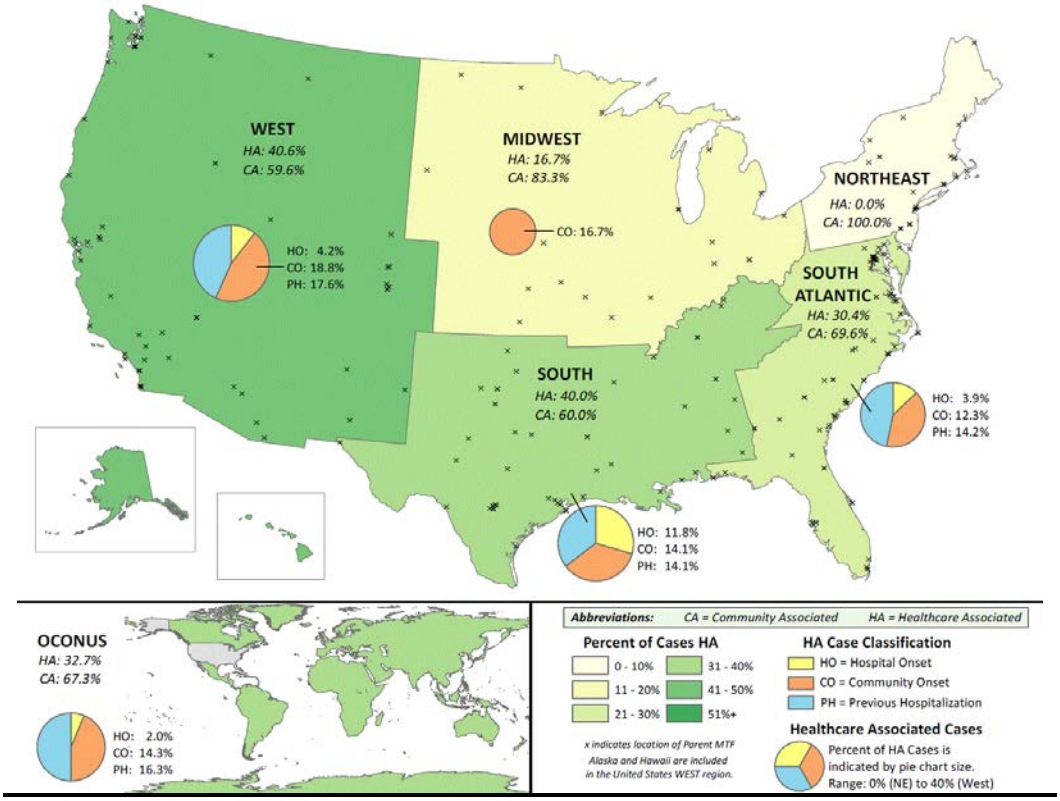
[a] Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.
[b] Admission MDRO prevalence included all individuals with an MDRO infection identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.
[c] Rates are not provided for these metrics due to low counts.
Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Regional Epidemiologic Infection Classifications

Among all *Acinetobacter* species prevalent infections identified in the MHS, 65% were CA and 35% were HA. Regionally, the US West had the highest percentage of *Acinetobacter* species HA cases followed closely by the US South (40.6% and 40.0%, respectively). The US Northeast and US Midwest had the largest percentage of CA cases (100% and 83.3%, respectively).

HA cases were further categorized into HO, CO, or previous hospitalization (PH) infections. Among all HA cases, the proportion classified as CO was 14.8%. The proportion of HA cases classified as HO was 4.8%, suggesting the infection was probably associated with the current hospitalization. PH cases, which indicated the patient had a hospitalization in the previous 12 months, comprised 14% of the total HA cases (data not shown). OCONUS locations and the US South Atlantic region had the highest proportion of PH cases (16.3% and 14.2%, respectively). However, CO cases were more prevalent in the US West and the US Midwest (18.8% and 16.7%, respectively) when compared to the US South Atlantic, US South, and US Northeast (Figure 3).

Figure 3. Proportion of Healthcare- and Community-Associated Cases among *Acinetobacter* Species Infections in the MHS by Region, CY 2015



Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases. Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

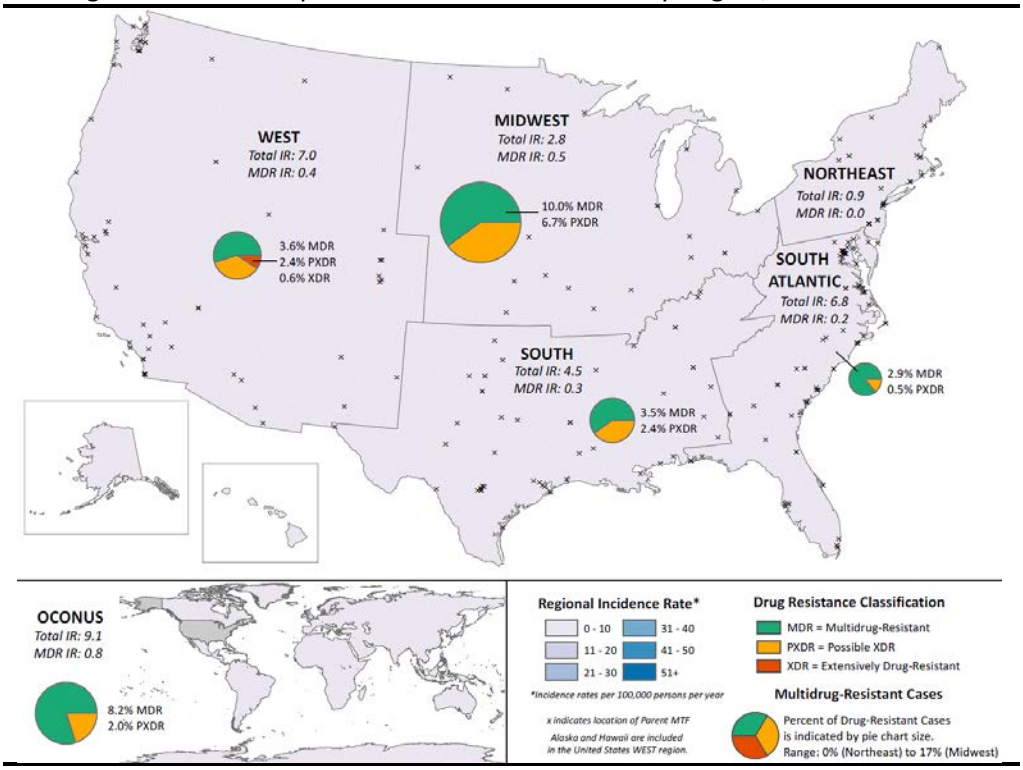
Section B – Antimicrobial Resistance and Use

Regional Multidrug Resistance

The 2015 annual incidence rate of MDR *Acinetobacter* infections was 0.3 per 100,000 persons per year. The highest regional incidence rate of MDR *Acinetobacter* infections was identified in OCONUS locations (0.8 per 100,000 persons per year). Among OCONUS infections, 8.3% were classified as MDR and 2.0% were classified as PXDR. OCONUS locations also had the highest total incidence rate (9.1 infections per 100,000 persons per year) of *Acinetobacter* infections. The second highest MDR incidence rate was reported in the US Midwest (0.5 per 100,000 persons per year); the US Midwest also reported the second highest total incidence rate (7.0 per 100,000 persons per year).

Ten percent of all *Acinetobacter* species infections identified in the US Midwest were classified as MDR and 6.7% were classified as PXDR. One XDR infection was identified in the US West, which accounted for 0.6% of all infections in the region (Figure 4). Across all regions, *Acinetobacter* species total incidence rates were less than 10 infections per 100,000 persons per year.

Figure 4. Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among *Acinetobacter* Species Infections in the MHS by Region, CY 2015



Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Antibiogram

The antibiogram for *Acinetobacter* species infections, from 2010 through 2015, is displayed in Table 6. In 2015, *Acinetobacter* species showed susceptibility to many of the antibiotics recommended for treatment. In 2015, *Acinetobacter* species showed the highest susceptibility to amikacin (97.5%), gentamicin (95.9%), and imipenem (97.5%). In 2015, *Acinetobacter* species displayed the lowest susceptibility to ceftriaxone (35.2%). Statistically significant trends for susceptibility were observed for amikacin, ampicillin/sulbactam, cefepime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, levofloxacin, meropenem, piperacillin, piperacillin/tazobactam, tetracycline, tobramycin, and trimethoprim/sulfamethoxazole (Table 6).

Table 6. Antibiogram of *Acinetobacter* Species Infections Identified in the MHS, CY 2010-2015

Antibiotics	2010	2011	2012	2013	2014	2015	Susceptibility Trend	Comment[a]
Amikacin	76.7	78.3	89.5	90.2	96.2	97.5	90 70	↑
Ampicillin/Sulbactam	88.0	80.1	88.6	91.6	93.8	91.9	100 80	↑
Cefepime	76.1	77.0	83.2	87.4	86.7	91.4	90 70	↑
Cefotaxime	44.0	54.0	46.9	58.7	61.0	62.8	60 40	
Ceftazidime	67.4	71.6	72.7	88.7	79.5	82.2	90 70	↑
Ceftriaxone	30.3	37.5	33.3	40.4	39.5	35.2	40 30	
Ciprofloxacin	77.3	78.1	86.2	89.7	93.1	93.7	90 70	↑
Doripenem	--	--	--	--	--	--		
Doxycycline	--	--	--	--	--	--		
Gentamicin	82.8	82.0	89.1	94.0	96.6	95.9	100 80	↑
Imipenem	80.6	77.6	87.4	91.9	95.2	97.5	95 75	↑
Levofloxacin	80.3	81.9	87.6	93.4	95.4	93.8	100 80	↑
Meropenem	67.2	78.5	66.7	86.8	89.7	94.8	85 65	↑
Minocycline	96.3	88.6	--	--	--	100.0		
Piperacillin	45.2	59.3	72.4	66.7	68.8	79.7	75 55	↑
Piperacillin/Tazobactam	76.8	67.4	83.0	83.1	87.0	88.0	90 70	↑
Tetracycline	85.3	78.5	90.3	92.8	88.9	88.8	100 80	↑
Ticarcillin/Clavulanate	--	--	--	--	--	--		
Tobramycin	77.0	81.4	88.1	93.0	96.4	94.2	95 75	↑
Trimethoprim/Sulfamethoxazole	82.8	77.8	81.9	88.7	90.9	88.2	90 70	↑

-- indicates that fewer than 30 isolates were tested.

[a] Arrow indicates the antibiotics with a significant change in direction of trend for significant two-tailed Cochrane-Armitage tests for trend established for a single antibiotic over time. A significant increase in susceptibility is denoted by a green upward arrow and a significant decrease in susceptibility is denoted by a blue downward arrow.

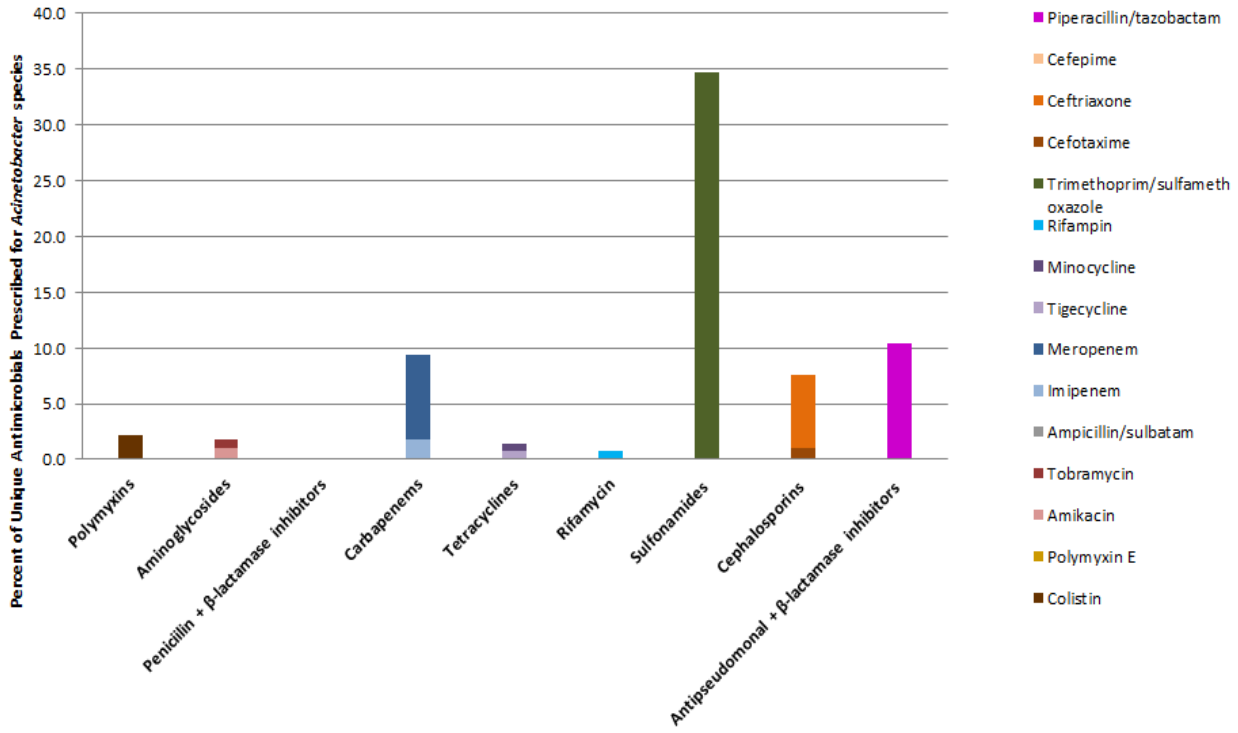
Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotic classes associated with *Acinetobacter* infections in 2015 were the folate pathway inhibitor/sulfonamide class (34.8%), anti-pseudomonal+β-lactamase inhibitors (10.4%), carbapenems (9.3%), and cephalosporins (7.6%). The remaining antibiotic classes were prescribed for less than 5% of infections in 2015 (Figure 5).

Figure 5. *Acinetobacter* Species Infection and Prescription Practices in the MHS, CY 2015



Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.
Data Source: NMCPHC HL7-formatted CHCS microbiology and HL7-formatted pharmacy databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Section C – Special Populations

There were no deployment-related infections among DON active duty service members during CY 2015.

Discussion

Findings show that *Acinetobacter* species infection rates within the MHS population in 2015 were above the weighted historic baseline and therefore above the threshold of expected variability. This could potentially mark a change in trend for *Acinetobacter* species infection in the MHS as the report from 2010-2014 documented a decreasing trend, with an overall decrease of 26%.[19] National trends for 2011-2014 also reported a decreasing trend, although the causes of this decrease are not known.[20] The possibility of a change in the direction of *Acinetobacter* infection trends, along with the documented tendency for *Acinetobacter* species to easily develop resistance to multiple antibiotics as described in in peer-review articles, underscores the importance of continued surveillance and careful monitoring of *Acinetobacter* species infections.[20]

Overall, *Acinetobacter* species infections in the MHS aligned with typical geographical and seasonal patterns. Climate and seasonality influence the transmission of *Acinetobacter* species, which flourish in geographic regions with warm, humid environments and climates, propagating increases in infections in the summer and early fall.[5,21,22] Consistent with literature, this analysis marks highest monthly incidence rates in the summer (July and August) and lowest rates in the winter months.[23] Consequently, the US West and US South Atlantic reported the highest incidence rates among all regions, which is not surprising given the warm environmental conditions in those locations.[23]

The assessment of exposure burden metrics of *Acinetobacter* species infections found that the admission MDRO prevalence rate was equal to the overall MDRO prevalence rate. This observation suggests that of all MDRO infections that occurred at any time during an admission, most were identified within the first three days of admission and were CO cases as opposed to HO cases. Although this finding aligns with HA analysis, it does not align with literature that reports HA *Acinetobacter* species infections as more common than CA cases.[5] Because the data indicated that 65% of MHS cases were CA, the majority of cases could be unrelated to prior or current contact with MTFs. This evidence lends credence to the previously suggested notion that community reservoirs might exist, although the natural reservoir of *Acinetobacter* species remains to be determined.[5]

The emergence of MDR *Acinetobacter* species is reported to be due to selective pressure from broad-spectrum antibiotics and transmission by patients in the hospital setting.[5] In the MHS in 2015, 6.1% of all prevalent *Acinetobacter* species infections were classified as multidrug-resistant. However, an estimated national proportion of MDR *Acinetobacter* was approximately 39.1% in 2015, a much larger proportion compared to the MHS population.[24] Within the MHS population, the major source of exposure for MDR *Acinetobacter* has changed due to fewer deployments to the Middle East.

Acinetobacter species infections in the MHS in 2015 maintained high susceptibilities to many tested antibiotics, indicating that several treatment options remain viable for this population. Imipenem and amikacin increased in efficacy over the surveillance period, maintaining the highest susceptibilities in 2015 (both at 97.5%). Other studies report 13% resistance (87%

susceptibility) to imipenem and 53% susceptibility to amikacin.[25] Aminoglycosides were prescribed for less than 5% of infections and carbapenems were prescribed for 10.4% of infections. These results are notable, as analysis identified these drugs are being prescribed less often for treatment, despite the highest rates of efficacy in the MHS. Consistent with literature, *Acinetobacter* species infections retain susceptibility to aminoglycosides and carbapenems, which remains one of the most important therapeutic options for *Acinetobacter* species.[25] The recent increases in susceptibilities could be explained by the low volume of MDR *Acinetobacter* deployment-related infections reported since the conclusion of OEF/OIF conflict in the Middle East.[25]

Current clinical guidelines for treating *Acinetobacter* infections recommend using imipenem, meropenem, ampicillin/sulbactam, colistin, tigecycline, or amikacin as first-line agents, as these antibiotics are the most effective against *Acinetobacter* species. However, this analysis identified that trimethoprim/sulfamethoxazole (TMP/SMX) was the most frequently prescribed antibiotic for *Acinetobacter* infections in the MHS beneficiary population. Additionally, some evidence suggests that TMP/SMX may be a questionable treatment option for *Acinetobacter* species infections due to variations in susceptibility.[26] This analysis found that *Acinetobacter* was 88.6% susceptible to TMP/SMX. It is possible that TMP/SMX is used in the MHS as an alternative treatment for polymyxin-resistant *Acinetobacter* infections; however, this analysis did not assess susceptibility patterns of polymyxins among *Acinetobacter* species infections due to testing counts below five.[26] Further analysis of TMP/SMX and polymyxin efficacy may be warranted in future annual reports.

In conclusion, this annual report summarized *Acinetobacter* species infection incidence and prevalence in the MHS beneficiary population in 2015 and reported upward trends from previous reports. Due to the increase in rates of *Acinetobacter* species infections, continued surveillance of *Acinetobacter* species within the MHS is encouraged.

Limitations

HL7-formatted data are generated within the CHCS at fixed MTFs; therefore, this analysis does not include microbiology records from purchased care providers, shipboard facilities, battalion aid stations, or in-theater facilities.

Microbiology data are useful for identifying laboratory-confirmed infections. However, infections that were treated presumptively without laboratory confirmation do not exist in the microbiology data. Clinical practice with regards to culturing varies between providers and facilities. Examples of situations where cultures may not be performed include confirmatory tests for patients with influenza-like illness (ILI) symptoms, or patients with superficial infections who are treated presumptively. Therefore, infection counts identified here may be an underestimate of the actual burden of *Acinetobacter* species in the MHS.

The data restructuring process for the analysis of clinical characteristics and antimicrobial resistance does not capture non-standard CHCS records. These non-standard records may include those containing the results of tests performed at reference laboratories or novel organism antibiotic combinations. The use of microbiology data for analysis of antibiotic resistance is also limited by the practice of cascade reporting, in which antibiotic sensitivity results are conditionally reported in CHCS to guide antimicrobial selection and treatment decisions. Cascade reporting is practiced to varying degrees at MHS MTFs.

The EDC data feed does not include records on medical encounters conducted outside the MHS (e.g., purchased care in the community) and it cannot be determined if an individual truly had no healthcare contact or other risk factors for *Acinetobacter* species infection, or if the individual had a risk factor that was not visible in the available data. Data on other factors commonly used to define HA cases were not available (e.g., presence of an invasive device, history of dialysis or surgery, a long-term care facility stay in the 12 months preceding the culture). Therefore, there may be HA cases currently miscategorized as CA cases. Without the ability to identify these HA cases, a more accurate estimate of CA cases could not be determined. Given the relatively healthy military population, however, any misclassification bias is likely minimal.

The pharmacy databases consist of outpatient non-intravenous prescriptions (outpatient), inpatient non-intravenous prescriptions (unit dose), and intravenous prescriptions (intravenous). Though treatment compliance in the inpatient setting can be assumed, outpatient pharmacy records indicate that a patient received a prescription and subsequent compliance is unknown. Due to near real-time data feeds, analysts are able to determine if a prescription was edited or canceled; however, the time difference between these events may allow for a short period of treatment not considered in this analysis. During ongoing surveillance efforts, patient treatment status may change as edited or canceled prescription records are received.

It is possible that not all antibiotic prescriptions were dispensed in response to an *Acinetobacter* species infection. Antibiotics that were prescribed within the appropriate timeframe to be associated with an *Acinetobacter* species specimen collection date may have actually been provided for reasons other than the documented infection, such as a different infection occurring

after *Acinetobacter* species was isolated. However, most antibiotics identified as being associated with an *Acinetobacter* species infection were antibiotics that are typically used to treat *Acinetobacter* species, so it is likely that the majority of prescriptions in this analysis were truly in response to the *Acinetobacter* species infection.

DMDC provides monthly snapshots of each active duty, reserve, and deployed Navy and Marine Corps service member's personnel record. Data are provided to DMDC by the service and analyses are dependent on the quality and completeness of these data. Any changes in service member status after the monthly data are extracted will not be captured until the following month. Active duty and reserve personnel records are maintained in separate databases, but activated reservists may be captured in the active duty DMDC file rather than the reserve DMDC file. Unit Identification Codes (UICs) reported for Marine Corps service members represent Reporting Unit Codes (RUCs), rather than UICs.

Personnel records for deployed service members are provided via CTS. The purpose of DMDC CTS is to capture personnel information for Central Command (CENTCOM) deployments. Additionally, deployment start and end dates are derived from the following systems and may not reflect the actual dates of deployment: Defense Finance Accounting System (DFAS), the Deployed Theater Accountability System (DTAS), the Secure Personnel Accountability System (SPA), historical PERSTEMPO files, and the Individual Personnel TEMPO Program. A country location of ZZ may represent shipboard or an unknown deployment location.

Infections may not be uniformly distributed within a spatial region; no distinctions were made with regard to the heterogeneity of incidence rates or prevalence among subunits (e.g., states, non-US countries). The choropleth maps represent an annual snapshot of infections and do not reflect the geographic movement of service members within the course of a year. Infections were georeferenced according to the locations of the MTFs where they were encountered, not according to the deployment locations or home locations of the service members. Map area does not equate to population size; parent MTF locations are displayed within US regions to convey the density of military medical facilities within each region.

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Appendix A: Antibiotics Used to Identify Resistance among *Acinetobacter* Species Infections in the MHS, CY 2015

Table A-1. Antibiotics Used to Identify Resistance among *Acinetobacter* Species Infections in the MHS, CY 2015

Antibiotic Class	Antibiotics Included in Class
Polymyxins	Colistin
	Polymyxin E
Aminoglycosides	Amikacin
	Tobramycin
Penicillin + β-lactamase inhibitors	Ampicillin/sulbactam
Carbapenem	Imipenem
	Meropenem
Tetracycline	Tigecycline
	Minocycline
Rifamycin	Rifampin
Sulfonamides	Trimethoprim/sulfamethoxazole
Cephalosporins	Cefotaxime
	Ceftriaxone
	Cefepime
Antipseudomonal + β-lactamase inhibitors	Piperacillin/tazobactam

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Appendix B: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
ABC	*Acinetobacter baumannii- calcoaceticus* complex
CA	community-associated
CDC	Centers for Disease Control and Prevention
CENTCOM	Central Command
CHCS	Composite Health Care System
CLSI	Clinical and Laboratory Standards Institute
CO	community-onset
CONUS	continental United States
CTS	Contingency Tracking System
CY	calendar year
DFAS	Defense Finance Accounting System
DMDC	Defense Manpower Data Center
DOD	Department of Defense
DON	Department of the Navy
DTAS	Deployed Theater Accountability System
EDC	EpiData Center Department
FMP	family member prefix
HA	healthcare-associated
HL7	Health Level 7 format
HO	hospital-onset
ICU	intensive care unit
IDSA	Infectious Disease Society of America
M2	Military Health System (MHS) Management Analysis and Reporting Tool
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MEPRS	Medical Expense and Performance Reporting System
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
PH	previous hospitalization
PXDR	possible extensively drug-resistant
PPDR	possible pandrug-resistant
PDR	pandrug-resistant
OCONUS	outside the continental United States
OIF	Operation Iraqi Freedom
OEF	Operation Enduring Freedom
OP	outpatient oral
RUC	Reporting Unit Code
SHEA	Society for Healthcare Epidemiology of America

Acronym/Abbreviation	Definition
SIDR	Standard Inpatient Data Record
SPA	Secure Personnel Accountability System
SSTI	skin and soft tissue infection
UD	unit dose
UIC	Unit Identification Code
US	United States
XDR	extensively drug-resistant